§ 446.81 Tetracycline hydrochloride.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Tetracycline hydrochloride is [4S-(4α,4aα,5aα,6β, 12aα)] - 4 - (dimethylamino) - 1,4,4a,5,5a,6,11,12a - octahydro - 3,6,10,12,12a - pentahydroxy - 6 - methyl - 1,11 - dioxo - 2 - naphthacenecarboxamide monohydrochloride. It is so purified and dried that:

(i) Its potency is not less than 900 micrograms per milligram.

(ii) [Reserved]

(iii) Its loss on drying is not more than 2 percent.

(iv) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 1.8 and not more than 2.8.

(v) When calculated on the anhydrous basis, its absorptivity at 380 nanometers relative to that of the tetracycline hydrochloride working standard similarly treated is 100±4 percent.

(vi) Its 4-epianhydrotetracycline content is not more than 2.0 percent.

(vii) It is crystalline.

(viii) It passes the identity test for tetracycline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, loss on drying, pH, absorptivity, 4-epianhydrotetracycline content, crystallinity, and identity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 0.1*N* hydrochloric acid to obtain a concentration of 1,000 micrograms of tetracycline hydrochloride per milliliter (estimated). Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.24 microgram of tetracycline hydrochloride per milliliter (estimated).

(2) [Reserved]

(3) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(5) *Absorptivity.* Dissolve approximately 40 milligrams of the sample, accurately weighed, in approximately 150 milliliters of distilled water by mixing thoroughly. Dilute to 250 milliliters with distilled water and mix thoroughly. Transfer a 10.0 milliliter aliquot of this solution to a 100-milliliter volumetric flask, add about 75 milliliters of distilled water and 5.0 milliliters of 5*N* NaOH, dilute to volume with water, and mix thoroughly. Treat a sample of the tetracycline hydrochloride working standard in the same manner. Exactly 6 minutes after the addition of the NaOH, determine the absorbance of each solution at 380 nanometers, using a suitable spectrophotometer and distilled water as the blank. Determine the percent absorptivity of the sample relative to the absorptivity of the standard using the following calculations:

$$\text{Percent relative absorptivity} = \frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times \frac{\text{Milligrams of standard}}{\text{Milligrams of sample}} \times \frac{\text{Potency of standard in micrograms per milligram}}{} \times \frac{10}{100 - m}$$

where: m = Percent moisture in the sample.

(6) *4-Epianhydrotetracycline.* Proceed as directed in § 436.309 of this chapter.

(7) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

(8) *Identity.* Proceed as directed in § 436.308 of this chapter.

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